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FORT KNOX, KENTUCKY

REPORT NO. 504

CESIUM-137 RETENTION AND DISTRIBUTION IN X-IRRADIATED RATS

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UNITED STATES ARMY
MEDICAL RESEARCH AND DEVELOPMENT COMMAND 4 September 1961

Report Submitted 1 September 1961

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2. Isotope Metabolism
3. Cesium-137

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CESIUM-137 RETENTION AND DISTRIBUTION IN X-IRRADIATED RATS

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4 September 1961

Effects of Low, Medium, and Massive Doses
Task 01
Biological and Medical Aspects of Ionizing Radiation
USAMRL Project No. 6X64-14-001

Report No. 504
USAMRL Project No. 6X64-14-001-01

ABSTRACT

CESIUM-137 RETENTION AND DISTRIBUTION IN X-IRRADIATED RATS

OBJECT

To study the influence of external ionizing radiation on the retention and distribution of the long-lived fission-product, cesium-137, in the rat.

RESULTS

Immediately following a total body exposure of 300, 600, and 900 r of 250 kv X-rays, rats were injected intraperitoneally with 1 μc solution of cesium-137. Rats given cesium-137 only served as controls. The X-irradiated rats excreted more cesium over the three-day period following irradiation exposure than did the control group. In a separate tissue distribution study, the largest part of the injected cesium dose was found in the muscle. Cesium was also concentrated to a smaller extent in the small intestine, liver, bone, and large intestine. The irradiated rats retained less cesium-137, expressed as mean per cent of injected dose, in muscle, bone, blood, small intestine, and spleen; whereas more cesium was held in the stomach and liver. The cesium content of whole organs was reflected, with the exception of stomach and spleen, to the same extent when considered on an organ unit-weight basis.

CONCLUSIONS

An analysis of the data indicated that the increased cesium excretion in the X-irradiated rats was primarily related to the greater urine volume (diuresis accompanied by increased water intake) in these rats resulting from radiation exposure. Increased urine excretion of cesium probably accounted for most of the lower values observed for cesium in the organs of the irradiated rats. The gastrointestinal concentrations of cesium-137 are explainable on the basis of gastric retention and delayed intestinal motility characteristic of the rat species following irradiation exposure. The liver concentration may be related to its corresponding weight increase following irradiation exposure; whereas the

spleen appeared to lose weight at a greater rate than it lost cesium. The failure of bone in the irradiated rats to take up cesium to the same extent as the control rats may be due to decreased blood concentration of cesium in these rats or it may reflect direct irradiation effects on the bone.

RECOMMENDATIONS

The cesium-137 concentration in the bone of X-irradiated rats should be studied for various radiation doses and for various times following irradiation exposure. The cesium-137 distribution in rats given a diuretic drug should be studied and compared with the findings reported in this study for X-irradiation exposure.

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CESIUM-137 RETENTION AND DISTRIBUTION IN X-IRRADIATED RATS

I. INTRODUCTION

Although the animal and human metabolism of fission-products has been extensively explored, the influence of external ionizing radiation on the uptake, distribution, and excretion of such elements has received comparatively little attention. Since both environmental exposure and clinical toxicity of these two sources of radiation may be interdependent, an experimental investigation of their combined short term effects in mammals has been undertaken.

Ulmer, Perkins, and Kereiakes (1) studied the distribution of iodine-131 in rats 24 hours after whole-body X-irradiation and found marked alterations compared to the isotope distribution in non-irradiated control animals. A reduction of 20 per cent in urinary and fecal loss of radioiodine occurred post-irradiation. As a consequence, increased radioactivity appeared in the blood, most of the organs, and particularly in the contents of the stomach and the pelt.

The present report is concerned with more detailed investigations of the retention and distribution of the longer-lived fission product, cesium-137, in rat tissue following whole-body radiation exposure.

II. EXPERIMENTAL

For exposure to whole-body X-irradiation the rats were placed two at a time in a shallow lucite cage. X-rays were delivered by a General Electric Maxitron Unit operated at 250 kvp, 30 ma, 4.75 mm Be inherent filtration, 1 mm Al + 0.5 mm Cu added filtration, HVL 1.1 mm Cu. The dose measured in air with a 250 r Victoreen Ionization Chamber was 140 r/min at a target-midline rat distance of 50 cm.

Cesium Retention

Male Sprague-Dawley rats weighing 160-250 grams were divided into the following groups: Cesium-137 injected only (controls), and cesium-137 with 300 r, 600 r, or 900 r whole-body radiation exposure.

Immediately following X-ray exposure the rats were injected intraperitoneally with 1 ml of a neutral aqueous solution containing 1 μc of cesium-137 (chemical form - CsCl). An aliquot of the solution was

set aside to be used as a standard. The rats were housed individually in metabolism cages to allow both separation and quantitative collection of urine and feces and accurate measurement of the water ingested. The rats were starved but were permitted water ad libitum. Control rats (those receiving cesium-137 but not irradiated) were handled in the same manner as the irradiated rats. Ten minutes after injection of the isotope the animal was placed in a glass tube (1-3/4 inches in diameter by 8 inches long) having holes at one end for air and a rubber stopper at the other end. The rat and tube were placed inside the well of a Nucleonic Corporation of America Supersensitive Large-Well Geiger-Counter (Fig. 1). The well in this counter measures 2 inches in diameter by 12 inches in length. This well-counter consists of multicylindrical elements with mesh walls concentrically arranged around the well. Its pulse size and shape are the same as the ordinary Geiger-Müller pulse. However, the above element arrangement overcomes to some extent the recognized limitations of the ordinary Geiger-counter, e. g., namely the insensitivity to gamma rays, long resolution time, and short life. The well-counter was connected to a Radiation Counter Laboratory Scaler and was shielded all around with 1-1/2 inches of lead.

The whole-body count measured 10 minutes after injection of cesium served as the control for each animal (i. e., the "100 per cent whole-body count"). Whole-body counts on each rat were repeated at 7 hours, and at 1, 2, and 3 days following injection. Total water ingestion, urine volume, and feces weight were measured each 24 hours. Aliquots of urine and digested feces (after digestion in nitric acid) were placed in test tubes and counted with a Radiation Counter Laboratory Well-Type Scintillation counter having a NaI (Tl) crystal.

Cesium Distribution

Male Sprague-Dawley rats weighing 170-220 grams were selected from litter mates taken after weaning and housed four to a cage until they attained the desired weight. Immediately after exposure to 900 r irradiation under the conditions described above, the two irradiated rats as well as two control (sham-irradiated) litter mates were injected intraperitoneally with a 1 ml saline solution containing 5 μc cesium-137. At the time of injection an aliquot of the cesium solution was set aside for use as a standard. The animals were then separately housed in metabolism cages. Food was withheld but water was given ad libitum.

Twenty-four hours after X-ray exposure the rats were lightly anesthetized with ether and killed by exsanguination from the abdominal

aorta. The major internal organs were removed intact. A muscle sample was taken from the left thigh while the right gonad and right femur were utilized for analysis. All organs were stripped of extraneous connective tissue, washed carefully, blotted dry, and weighed. The contents of the stomach, small intestine, and large intestine were included in the analyses of these organs; feces were added to the contents of the large intestine. Whole organs or 1 to 2 gram portions were weighed and taken for analysis. All samples were wet ashed in hot concentrated nitric acid and diluted as necessary for counting. Samples were counted in a volume of 3 ml in the well-type scintillation counter described above.

For final calculations, muscle was considered to constitute 45 per cent of whole-body weight and blood volume 5.3 ml per 100 gram body weight; bone weight was estimated from standard tables (2).

III. RESULTS

Cesium Retention

The results of the retention study are shown in Tables 1 and 2. Rats receiving cesium-137 only will be referred to as the control group. The body weight of the control group (food withheld) decreased to 77.7 per cent of the initial body weight in 3 days; whereas the body weight of the irradiated rats decreased to 74.3 to 77.2 per cent of their initial weight during this time interval.

Exposure to ionizing radiation significantly alters the retention of cesium-137 by the body of the rat. The whole-body content of this isotope at 7, 24, 48, and 72 hours after exposure to irradiation of 300 r to 900 r is shown graphically in Figure 2. Uniformly, and from the time of earliest measurement, the irradiated animal retained less cesium-137 than did the corresponding non-irradiated controls. Moreover, this response to irradiation was of progressively greater significance with time, being most marked on the final day of observation. The effect was not directly proportional to radiation dose, however, being maximal in those animals exposed to 600 r.

As a necessary corollary, exposure to ionizing radiation should significantly increase the rate of elimination of cesium in rats. This is demonstrated by measurement of urinary cesium-137 radioactivity (Fig. 3). In all instances, urinary excretion of the isotope is increased subsequent to X-irradiation. Excretion by this route was maximal on

the first day after exposure to X-ray (up to 12 per cent of the injected isotope) and fell off rapidly thereafter. The quantity of radioactivity in the feces was small, amounting to less than 1 per cent of the injected dose of cesium for both groups and appeared to be proportional to the volume of fecal material (Tables 1 and 2).

Cesium Distribution

The data are expressed as 1) mean per cent of injected dose per total organ, and 2) mean concentration of radioactivity (counts per second per gram of sample divided by counts per second injected per gram of body weight) (3). The latter values are calculated to compensate for changes in organ weight and variations in body weight. These results are given in Table 3 along with calculations for the "t" test and probability values.

In both control and X-irradiated animals the greater portion of the injected isotope was found in muscle. Analyses of the other tissues indicated that cesium was also concentrated, but, to a lesser extent, in the small intestine, liver, bone, and large intestine. The data for all the tissues studied are shown graphically in Figure 4.

Irradiated rats retained less cesium-137 in the muscle than did control rats, probably reflecting increased cesium excretion into the urine. As in the retention study the total urine volume was uniformly greater in the irradiated rats and was accompanied by increased content of cesium-137. There was a correspondingly greater ingestion of water in irradiated animals. The blood concentration of cesium was significantly higher in the control rats. There was no significant difference between the two groups in the 24 hour cesium content of gonads, heart, kidneys, and large intestine. Bone, small intestine, and spleen retained less cesium in the irradiated rats, while the liver and stomach contained greater concentrations of the isotope.

The distribution of cesium was, in general, unchanged when calculated on a unit weight basis. Two exceptions were the spleen and the stomach plus contents. On a unit weight basis, the spleen retained more and the stomach less cesium in the irradiated rats.

IV. DISCUSSION

Cesium-137 has a half-life of 30 years and emits 1.17 Mev (8 per cent) and 0.51 Mev (92 per cent) beta particles followed by 0.662 Mev

gamma rays. As one of the alkali metals, it would be predicted that the organ distribution of cesium should resemble that of potassium. In this regard excretion and distribution studies with the fission products, cesium-135 and cesium-138, were reported by Hamilton (4), who found a relatively high accumulation in the soft tissues, especially muscle, and a low uptake in the skeleton. Absorption from the intestinal tract was found to be 100 per cent after ingestion with about 50 per cent being excreted within 10 days.

Hood and Comar (5, 6) studied the metabolism of cesium-137 in the rat. Cesium was widely distributed in the body. Skeletal accumulation, represented by isotope concentration in the femur, was found to be quite small. The greatest accumulation and most tenacious retention was in muscle tissue, although this tissue accumulated cesium at a slightly lower rate over the first week than did liver, spleen, and kidney. Blood always had the lowest concentration, so the tissues may have taken up cesium against a concentration gradient.

Ballou and Thompson (7) investigated the effect of acute and chronic administration of cesium-137 in rats. The experiments on acute administration of the element were of particular interest to the present discussion. After a single dose the retention of cesium-137 was followed in eleven organs and tissues for a period of 200 days. Muscle was again found to be the critical organ.

The present study both confirms results in the distribution of cesium reported by other workers and extends these data to encompass the effect of the added stress of external whole-body irradiation exposure. The results clearly indicate a greater excretion of cesium-137 in the irradiated rats, quite probably related to the increased urinary volume in these animals. Hence a major increase in the excretion of this isotope apparently may be brought about by inducing diuresis. To ascertain if, indeed, such urinary losses of cesium in irradiated animals exceeded the control values primarily as a function of increased urinary volume, the observations for the 3 days were pooled and normalized by assuming that the number of counts per urine sample was a constant fraction of the urine volume. The difference between the observed urine counts and those predicted on the basis of the changes in urinary volume were then obtained. There was no significant difference between the observed and predicted urine counts, strongly suggesting that the urinary losses of cesium in the irradiated animals and increased urinary volume are causally related phenomena.

The water metabolism in the rat following X-irradiation has been studied by Edelmann (8, 9). Both ingestion and excretion of water are increased on the first day after irradiation and are proportional to log dose, at least in the range of 75 r to 600 r. If the fluid intake was restricted for 24 hours immediately following irradiation, urinary volume still increased. Hence Edelmann felt that diuresis preceded and may, in fact, be the cause of polydipsia. Serum taken from the irradiated rats within 24 hours after exposure to irradiation and assayed for an "antidiuretic substance," probably the antidiuretic factor of the posterior lobe of the pituitary gland, was found to contain smaller concentrations of this substance than did the serum of unirradiated controls. At least the first period of diuresis, therefore, coincides with a decreased amount of circulating antidiuretic substance. It would appear that cesium in body water would be markedly affected by this diuresis and the concomitantly increased water intake contributing, in a great part, to the differences in the excretion of the element.

If the tissue deposition of cesium is examined further, several interesting features are noted. In general, the organs of irradiated animals contained less cesium, as would be predicted from the greater urinary losses in this group (Table 3). The increased gastrointestinal concentration of cesium, probably due to gastric retention and delayed intestinal motility (10, 11), may also influence the distribution pattern. Although there is more total cesium in the stomach of irradiated animals than in the control group, it is more dilute and accounts for the lesser cesium concentration in the adjoining small intestine. The variations in concentrations of cesium in the liver and spleen are most likely related to weight changes in these organs subsequent to irradiation. The liver weight increased by 24 per cent at 24 hours in the irradiated rats. It has been postulated that such a post-irradiation increase in liver size is due to an increase in glycogen storage (12). The mean weight of the spleens in the irradiated rats decreased by about 50 per cent at 24 hours. It would appear that the spleen in these animals lost weight at a greater rate than it lost cesium.

Of considerable interest is the striking failure of bone in the irradiated animal to take up cesium at 24 hours to the extent which occurs in the control animal. The concentrations in bone may be due to decreased blood concentration of cesium in these rats or it may reflect direct irradiation effects on bone. A further detailed study of this phenomenon is warranted.

V. CONCLUSIONS

An analysis of the data indicated that the increased cesium excretion in the X-irradiated rats was primarily related to the greater urine

volume (diuresis accompanied by increased water intake) in these rats resulting from radiation exposure. Increased urine excretion of cesium probably accounted for most of the lower values observed for cesium in the organs of the irradiated rats. The gastrointestinal concentrations of cesium-137 are explainable on the basis of gastric retention and delayed intestinal motility characteristic of the rat species following irradiation exposure. The liver concentration may be related to its corresponding weight increase following irradiation exposure; whereas the spleen appeared to lose weight at a greater rate than it lost cesium. The failure of bone in the irradiated rats to take up cesium to the same extent as the control rats may be due to decreased blood concentration of cesium in these rats or it may reflect direct irradiation effects on the bone.

VI. RECOMMENDATIONS

The cesium-137 concentration in the bone of X-irradiated rats should be studied for various radiation doses and for various times following irradiation exposure.

The cesium-137 distribution in rats given a diuretic drug should be compared with the findings reported in this study for X-irradiation exposure.

VII. REFERENCES

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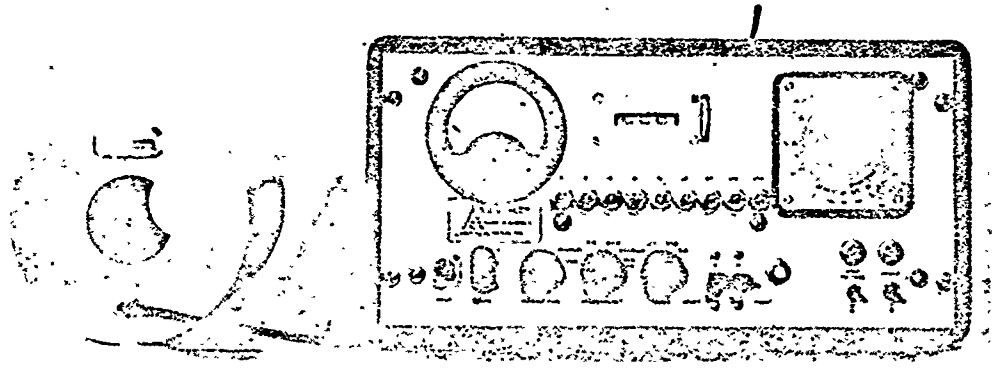

Fig. 1. Small animal whole-body counting arrangement.

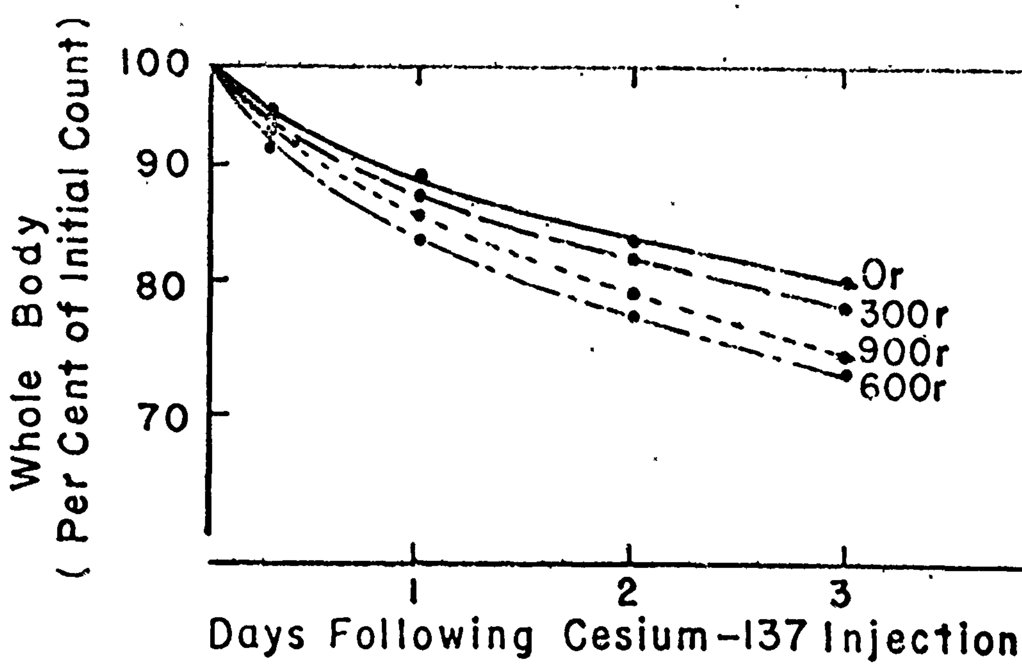

Fig. 2. Cesium-137 retention in starved control and X-irradiated rats.

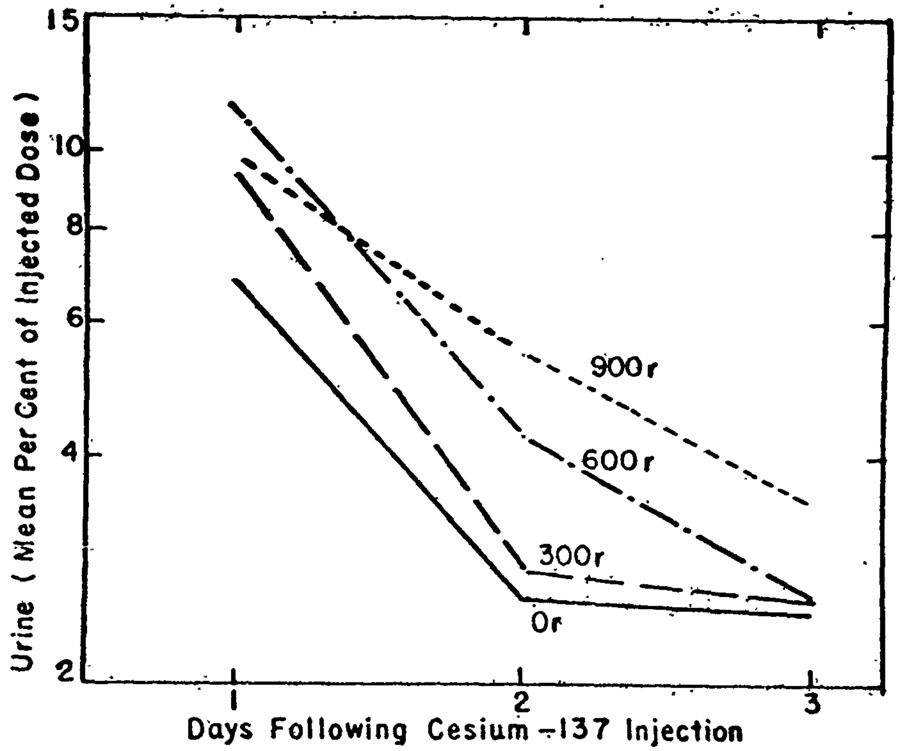

Fig. 3. Urine excretion of cesium-137 (mean per cent of injected dose) in starved control and X-irradiated rats.

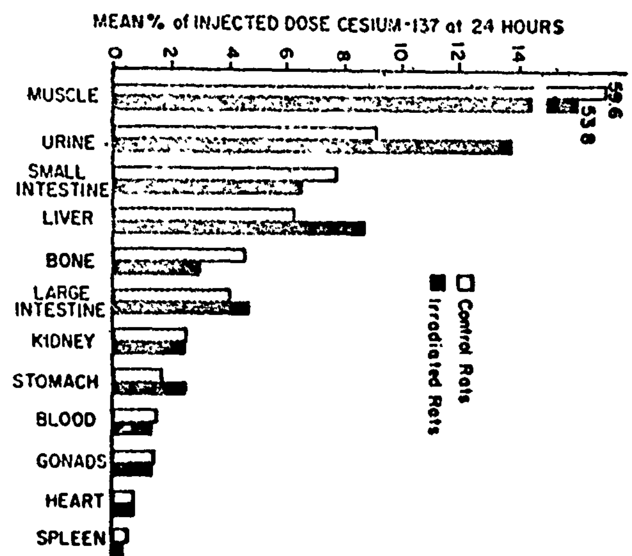

Fig. 4. Twenty-four hour distribution of cesium-137 in starved control and X-irradiated rats.

TABLE 1

EFFECT OF STARVATION IN X-IRRADIATED RATS

Condition	Time Following Exposure	Body Weight	Feces Weight	Urine Volume	Water Intake
	days	grams	grams	ml	ml
Cesium-137 only	1	88.8 ± 1.9 (18)*	1.07 ± .54 (17)*	17 ± 7 (17)*	13 ± 8 (17)*
	2	82.9 ± 2.5 (18)	.42 ± .30 (17)	6 ± 3 (15)	7 ± 4 (15)
	3	77.7 ± 3.0 (18)	.32 ± .18 (17)	4 ± 3 (17)	4 ± 2 (9)
Cesium-137 and 300 r	1	88.9 ± 1.5 (9)	.31 ± .28 (9)	29 ± 11 (10)	22 ± 11 (10)
	2	82.7 ± 1.5 (10)	.31 ± .18 (9)	8 ± 6 (10)	9 ± 7 (10)
	3	76.8 ± 2.2 (10)	.76 ± .41 (10)	4 ± 4 (10)	3 ± 3 (10)
Cesium-137 and 600 r	1	91.0 ± 1.6 (13)	.39 ± .20 (12)	41 ± 15 (14)	45 ± 13 (13)
	2	83.2 ± 2.1 (14)	.34 ± .30 (12)	22 ± 12 (14)	18 ± 10 (12)
	3	77.2 ± 2.4 (14)	.54 ± .23 (14)	5 ± 4 (14)	6 ± 4 (14)
Cesium-137 and 900 r	1	88.2 ± 2.3 (19)	.46 ± .40 (17)	51 ± 19 (11)	44 ± 26 (16)
	2	80.4 ± 3.4 (19)	.38 ± .38 (14)	26 ± 11 (7)	26 ± 12 (18)
	3	74.3 ± 3.3 (18)	.40 ± .20 (17)	8 ± 3 (10)	7 ± 5 (19)

*Numbers in parenthesis indicate number of rats.

TABLE 2

CESIUM-137 RETENTION IN X-IRRADIATED RATS

Condition	Time Following Exposure	Total Body	Urine	Feces
	days	% of injected	% of injected	% of injected
Cesium-137 only	.007	94.5 ± 2.9 (18)*	.	.
	1	88.7 ± 1.9 (17)	6.8 ± 1.8 (16)*	0.8 ± 0.4 (12)*
	2	84.5 ± 2.8 (17)	2.6 ± 0.4 (13)	0.5 ± 0.3 (13)
	3	79.8 ± 2.9 (17)	2.5 ± 1.4 (16)	0.4 ± 0.2 (16)
Cesium-137 and 300 r	.007	94.8 ± 0.9 (8)	.	.
	1	87.3 ± 1.5 (9)	9.4 ± 1.3 (10)	0.2 ± 0.1 (8)
	2	83.7 ± 1.4 (9)	2.8 ± 0.8 (10)	0.4 ± 0.2 (10)
	3	78.2 ± 1.3 (8)	2.0 ± 0.8 (10)	0.6 ± 0.3 (9)
Cesium-137 and 600 r	.007	91.7 ± 1.8 (13)	.	.
	1	83.4 ± 1.9 (13)	11.7 ± 2.5 (14)	0.4 ± 0.3 (13)
	2	77.4 ± 2.9 (13)	4.3 ± 0.6 (13)	0.4 ± 0.2 (13)
	3	73.4 ± 2.9 (13)	2.6 ± 0.6 (13)	0.4 ± 0.2 (14)
Cesium-137 and 900 r	.007	93.8 ± 1.8 (18)	.	.
	1	87.1 ± 3.0 (18)	9.7 ± 2.3 (18)	0.4 ± 0.4 (18)
	2	80.0 ± 3.5 (18)	5.5 ± 1.1 (14)	0.3 ± 0.3 (14)
	3	74.5 ± 3.9 (18)	3.4 ± 0.8 (17)	0.4 ± 0.3 (18)

*Numbers in parenthesis indicate number of rats.

TABLE 3

CESIUM-137 DISTRIBUTION IN RAT TISSUES AT 24-HOURS POST-ADMINISTRATION

Organ or Body Fluid	Per Cent Dose per	Mean Per Cent of Dose Injected: No. Rats	Control	No. Rats	X-irradiated	t	P	Mean Concentration of Radioactivity: No. Rats	Control	No. Rats	X-irradiated	t	P
Blood	Total Volume	22	1.41 ± .23	21	1.23 ± .13	3.21	< 0.01	21	.26 ± .05	21	.23 ± .03	2.59	0.01
Bone	Organ	21	4.49 ± .72	20	2.94 ± .67	7.15	< 0.01	22	.71 ± .13	20	.44 ± .10	7.52	< 0.01
Gonads	Organ (both)	22	1.32 ± .28	20	1.26 ± .21	0.90	> 0.05	21	.95 ± .15	22	.93 ± .21	0.30	> 0.05
Heart	Organ	21	.67 ± .11	22	.67 ± .12	0.03	> 0.05	21	2.04 ± .30	21	1.96 ± .38	0.07	> 0.05
Kidney	Organ (both)	21	2.46 ± .55	21	2.37 ± .42	0.57	> 0.05	21	2.74 ± .55	22	2.66 ± .42	0.57	> 0.05
Large intestine	Organ & contents	22	3.96 ± 1.26	20	4.61 ± 2.17	1.18	> 0.05	20	1.44 ± .45	17	1.73 ± .71	1.44	> 0.05
Liver	Organ	22	6.24 ± 1.64	21	8.72 ± 1.38	5.48	< 0.01	22	1.76 ± .28	22	2.04 ± .43	2.58	0.01
Muscle	Organ	22	59.60 ± 9.03	22	53.80 ± 8.46	2.21	0.04	22	1.32 ± .21	22	1.20 ± .19	2.15	0.04
Small Intestine	Organ & contents	21	7.69 ± 1.31	22	6.42 ± 1.39	3.10	< 0.01	22	2.35 ± .47	22	2.11 ± .45	1.74	> 0.05
Spleen	Organ	21	.44 ± .10	20	.25 ± .06	8.00	< 0.01	22	1.67 ± .41	21	1.91 ± .30	2.27	0.03
Stomach	Organ & contents	20	1.66 ± .38	22	2.34 ± 1.43	2.15	0.04	21	2.26 ± .74	18	1.20 ± .34	5.91	< 0.01
Urine	Total Volume	22	9.15 ± 2.83	22	13.77 ± 5.10	3.71	< 0.01						

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